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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Intellectual Property Department
Amylin Pharmaceuticals, Inc.
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EXAMINER	
DEVI, SARVAMANGALA J N	
ART UNIT	**PAPER NUMBER**
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/445,517	DUFT ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10/23/07*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-29,31-39,68-80,82 and 84-97* is/are pending in the application.

4a) Of the above claim(s) *25, 26, 28, 35, 36, 69-71, 73-75, 77-79 and 85-94* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23,24,27,29,31-34,37-39,68,72,76,80,82,84 and 95-97* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/23/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO APPLICANTS' AMENDMENT

Applicants' Amendment

1) Acknowledgment is made of Applicants' amendment filed 10/23/07 in response to the final Office Action mailed 04/23/07. With this, Applicants have amended the claims.

Status of Claims

2) Claims 23, 33 and 76 have been amended via the amendment filed 10/23/07.

Claims 23-29, 31-39, 68-80, 82 and 84-97 are pending.

Claims 23, 24, 27, 29, 31-34, 37-39, 68, 72, 76, 80, 82, 84 and 95-97 are under examination.

Information Disclosure Statement

3) Acknowledgment is made of Applicants' information disclosure statement filed 10/23/07. Except for the reference of Chapman *et al.*, which is not submitted, the information referred to therein has been considered and a signed copy is attached to this Office Action.

Prior Citation of References

4) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Rejection(s) Maintained

5) The provisional rejection of the instant claims made in paragraph 26 of the Office Action mailed 05/30/06 and maintained in paragraph 31 of the Office Action mailed 04/23/07 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-16 of the co-pending application, SN 09/870,762, is maintained for reasons set forth therein. Applicants' statement that they are willing to consider submitting a terminal disclaimer in the present application with regard to the '762 application should this application issue as a patent prior to the present application, has been noted.

6) The provisional rejection of claims 33 and 82 made in paragraph 28 of the Office Action mailed 05/30/06 and maintained in paragraph 32 of the Office Action mailed 04/23/07 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 6

of the co-pending application, 10/851,574, is maintained for reasons set forth therein. Applicants' statement that they are willing to consider submitting a terminal disclaimer in the present application with regard to the '574 application should this application issue as a patent prior to the present application has been noted.

Rejection(s) Withdrawn

7) The rejection of claims 68, 72, 76, 84 and 97 made in paragraph 35 of the Office Action mailed 05/30/06 and made and/or maintained in paragraph 33 of the Office Action mailed 04/23/07 under 35 U.S.C § 112, first paragraph, as being non-enabled with regard to the scope, is withdrawn in light of Applicants' amendment to the claims. Applicants' arguments have been considered, but are moot in light of the rejection set forth below under paragraph 24 and the reasoning provided therein.

8) The rejection of claims 23, 24, 33 and 34 made in paragraph 34 of the Office Action mailed 04/23/07 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 34 and 35 of the US patent 5,686,411 issued to Gaeta *et al.* ('411, already of record) as evidenced by Tsanev (*Vutr. Boles* 23: 12-17, 1984, abstract), is withdrawn in light of Applicants' amendment to the claims and/or the base claims. Applicants' arguments have been considered, but are moot in light of the modified rejection set forth below under paragraph 21 and the reasoning provided therein.

9) The rejection of claims 23 and 33 made in paragraph 35 of the Office Action mailed 04/23/07 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 11 and 13 of US patent 5,321,008 issued to Beumont *et al.* as evidenced by Tsanev (*Vutr. Boles* 23: 12-17, 1984, abstract, already of record) and Rink *et al.* (US 5,739,106, already of record) ('106), is withdrawn in light of Applicants' amendment to the claims and/or the base claims. Applicants' arguments have been considered, but are moot in light of the modified rejection set forth below under paragraph 22 and the reasoning provided therein.

10) The rejection of claims 23, 33 and 76 made in paragraph 36 of the Office Action mailed 04/23/07 under 35 U.S.C § 112, first paragraph, as containing new matter, is withdrawn upon further consideration. A modified rejection is set forth below in paragraph 23 to address claim 33, as amended.

11) The rejection of claims 23, 24, 27, 29, 31-34, 37-39, 80, 82, 95 and 96 made in paragraph 37 of the Office Action mailed 04/23/07 under 35 U.S.C § 112, first paragraph, as being non-enabled with regard to the scope, is withdrawn in light of Applicants' amendment to the claims. Applicants' arguments have been considered, but are moot in light of the rejection set forth below under paragraph 24 and the reasoning provided therein.

12) The rejection of claims 23, 33 and 76 made in paragraph 38(a) of the Office Action mailed 04/23/07 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claims.

13) The rejection of claim 23 made in paragraph 38(b) of the Office Action mailed 04/23/07 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

14) The rejection of claim 33 made in paragraph 38(c) of the Office Action mailed 04/23/07 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

15) The rejection of claims 23 and 33 made in paragraph 38(d) of the Office Action mailed 04/23/07 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claims.

16) The rejection of claims 24, 27, 29, 31, 32, 34, 37-39, 68, 72, 80, 82, 84 and 95-97 made in paragraph 38(e) of the Office Action mailed 04/23/07 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the base claim(s).

17) The rejection of claims 23, 24, 27, 29, 31, 33, 34, 37-39, 80 and 82 made in paragraph 39 of the Office Action mailed 04/23/07 under 35 U.S.C § 102(b) as being anticipated by Kolterman *et al.* (WO 96/40220, already of record) ('220) as evidenced by Tsanev (*Vutr. Boles* 23: 12-17, 1984, abstract, already of record), is withdrawn in light of Applicants' amendment to the claims and/or the base claims. Applicants' arguments have been considered, but are moot in light of the modified rejection set forth below under paragraph 26 and the reasoning provided therein.

18) The rejection of claims 23, 24, 29, 33, 34 and 38 made in paragraph 40 of the Office Action mailed 04/23/07 under 35 U.S.C § 102(e)(2) as being anticipated by Gaeta *et al.* (US

5,686,411, already of record) ('411) as evidenced by Tsanev (*Vutr. Boles* 23: 12-17, 1984, abstract, already of record), is withdrawn in light of Applicants' amendment to the claims and/or the base claims. Applicants' arguments have been considered, but are moot in light of the modified rejection set forth below under paragraph 27 and the reasoning provided therein.

19) The rejection of claims 23, 24, 27, 29, 31, 33, 34, 37-39, 80 and 82 made in paragraph 41 of the Office Action mailed 04/23/07 under 35 U.S.C § 102(b) as being anticipated by Kolterman *et al.* (*Diabetologia* 39: 492-499, April, 1996, already of record) (Kolterman *et al.*, 1996) as evidenced by Itasaka *et al.* (*Psychiatr. Clin. Neurosci.* 54: 340-341, June 2000), is withdrawn in light of Applicants' amendment to the claims and/or the base claims. Applicants' arguments have been considered, but are moot in light of the modified rejection set forth below under paragraph 28 and the reasoning provided therein.

20) The rejection of claims 23, 24, 27, 29, 33, 34, 37 and 38 made in paragraph 42 of the Office Action mailed 04/23/07 under 35 U.S.C § 102(e)(2) as being anticipated by Beumont *et al.* (US 5,321,008, already of record) ('008) as evidenced by Tsanev (*Vutr. Boles* 23: 12-17, 1984, abstract, already of record), is withdrawn in light of Applicants' amendment to the claims and/or the base claims. Applicants' arguments have been considered, but are moot in light of the modified rejection set forth below under paragraph 29 and the reasoning provided therein.

New Rejection(s) Necessitated by Applicants' Amendment

Double Patenting Rejection(s)

21) Claims 23, 24, 33 and 34 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 34 and 35 of the US patent 5,686,411 issued to Gaeta *et al.* ('411, already of record) as evidenced by Tsanev (*Vutr. Boles* 23: 12-17, 1984, abstract). Although the conflicting claims are not identical, they are not patentably distinct from each other.

The method of treatment claimed in claims 34 and 35 of the '411 patent includes administering to a mammal with diabetes mellitus a therapeutically effective amount of the amylin agonist of claim 19, ^{25,28,29}Pro-human amylin (SEQ ID NO: 1 or pramlintide). The portion of the disclosure of the '411 patent at lines 45-53 in column 7 supporting the limitation 'mammal' does

not exclude, but expressly includes a patient seen by a medical practitioner, i.e., a human. The portion of the disclosure of the '411 patent at second paragraph under 'Summary of the Invention' supporting the limitations 'diabetes mellitus' and 'administration of .... an amylin agonist analogue' include insulin-requiring diabetes mellitus and administration of an amylin agonist analogue alone (i.e., consisting of) or in conjunction with insulin or a glucagon, i.e., not in conjunction with another obesity relief agent. The portion of the disclosure of the '411 patent at lines 53-59 in column 8 supporting the limitation 'therapeutically effective amount' of the amylin agonist includes the dosage units of 0.1 to 5 mg or 0.5 to 1.0 mg of the amylin agonist. The amount effective to treat obesity encompassed in the instant claims as described in the instant application of about 0.01 milligrams to about 5 milligrams per day falls within the range disclosed in the '411 patent. Given the art-known prevalence of intrinsic obesity in 80% to 90% of diabetic patients as disclosed by Tsanev, at least one of the human diabetic patients used in the method disclosed in the '411 patent qualifies as a human patient in need of treatment for obesity. Therefore, the method of the '411 patent comprising or consisting of the administration of 0.1 to 5 mg, or 0.5 to 1.0 mg of the amylin agonist, ^{25,28,29}Pro-human amylin alone or in conjunction with insulin or glucagon, to a diabetic human anticipates the instant claims. Given that the method step of the '411 patent and the instant claims are the same, the amylin agonist analogue pramlintide used and its amount administered are the same, and the human diabetic patient used is the same, the method of the '411 patent is expected to bring about obesity-treating effect in the intrinsically obesity diabetic patient administered with a therapeutically effective amount of the pramlintide as claimed in the instant invention. Since the structural limitations of the instantly claimed method and all of the criteria required by the instant claims are met by the disclosure of Gaeta *et al.* ('411), Gaeta's ('411) method is expected to serve necessarily as the instantly claimed method and is expected to bring about the obesity-treating effect.

22) Claims 23 and 33 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 11 and 13 of US patent 5,321,008 issued to Beumont *et al.* as evidenced by Tsanev (*Vutr. Boles* 23: 12-17, 1984, abstract, already of record) and Rink *et al.* (US 5,739,106, already of record) ('106). Although the conflicting claims are not identical, they are not patentably distinct from each other.

The method of treatment claimed in claims 11 and 13 of the '008 patent includes administering to a human with type 2 diabetes mellitus a therapeutically effective amount of the amylin agonist calcitonin. The portion of the disclosure of the '008 patent at lines 14-17 in column 5; lines 8-11 and 49-54 in column 12; and lines 34 and 35 in column 2 that supports the claims includes subcutaneous administration to an insulin-requiring human who suffers from Type 1 or Type 2 diabetes mellitus a therapeutically effective amount of an amylin agonist *alone* such as calcitonin (i.e., consisting of), or calcitonin and insulin (i.e., comprising) contained in a pharmaceutically acceptable carrier. The portion of the disclosure of the '008 patent at first full paragraph in column 13 of the '008 patent supporting the 'therapeutically effective amount' includes the typical dosage units of about 0.1 to 1 mg of calcitonin. The amount effective to treat obesity, the amount effective to obesity encompassed in the instant claims as described in the instant application of about 0.01 milligrams to about 5 milligrams per day falls within the range of the therapeutically effective amount disclosed in the '008 patent. Given the art-known prevalence of intrinsic obesity in 80% to 90% of diabetic patients as disclosed by Tsanev (see abstract), at least one insulin-requiring human diabetic patient used in the method disclosed in the above-identified claims claimed in the '008 patent qualifies as a human patient in need of treatment for obesity. Therefore, the method of the '008 patent comprising or consisting of the administration of about 0.1 to 1 mg of calcitonin to an insulin-requiring diabetic human anticipates the instant claims. Given that the method step of the '008 patent and the instant claims is the same, and the amylin agonist calcitonin administered and the amount administered are the same, and the human diabetic patient to whom calcitonin is administered is the same as the one described in the instant application, the method claimed in the '008 patent is expected to bring about an obesity-treating effect in the intrinsically obese calcitonin-treated diabetic patient of the '008 patent. Since the structural limitations of the instantly claimed method and all of the criteria required by the instant claims are met by the teachings of the '008 patent, Beumont's ('008) method is expected to serve necessarily as the instantly claimed method and is expected to bring about the obesity-treating effect. The art-recognized intrinsic obesity being prevalent in 80 to 90% of diabetic patients as disclosed by Tsanev (see abstract), Beumont's ('008) method of administration of the above-identified therapeutically effective amount (i.e., dosage units of about 0.1 to 1 mg) of the amylin agonist calcitonin to at least one intrinsically obese type 2

diabetic human subject anticipates the instant claims.

Rejection(s) under 35 U.S.C. § 112, First Paragraph (New Matter)

23) Claim 33 and the dependent claims 34, 37-39, 72, 80, 82 and 96 are rejected under 35 U.S.C § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 33, as amended, includes the new limitation: treat obesity 'in said human subject' and 'and wherein said human subject is in need of treatment for obesity' and continues to include the limitation: 'method of treating obesity .... consisting of administering'. A method of treatment of obesity 'consisting of' such an administration step *excludes,* for example, simultaneous insulin administration, or insulin administration minutes or hours before or after the administration. However, neither the original claims, nor the description of the novel methods of treatment of the instant invention support such a method of treating obesity 'consisting of' administering an amount a composition effective to treat obesity in said human subject comprising an obesity relief agent consisting of an amylin or an amylin agonist and a pharmaceutically acceptable carrier. For example, the originally filed specification at lines 10-13 of page 12 of the specification states [Emphasis added]:

> The present invention is directed to novel methods for treating or preventing obesity in humans *comprising* the administration of an amylin or an amylin agonist, the amylin agonist analogue ^{25,28,29}Pro-human amylin.

Pages 28-29 and Table I describe a statistically significant reduction in the mean baseline weight seen after the subcutaneous administration of 60 micrograms TID or 60 micrograms QID of one specific amylin agonist analogue species, pramlintide, to type II diabetic subjects for four weeks, wherein said pramlintide administration was accompanied *with the continued administration of insulin.* The method of treatment of obesity as described in the originally filed specification comprised insulin treatment *and* the administration of a specific dose of pramlintide to type II diabetic patients. This however does not provide descriptive support for the now claimed method of treating obesity in a human in need of treatment for obesity, said method 'consisting' of administering to said subject an

amount of a composition as recited comprising an amylin or any amylin agonist and a pharmaceutically acceptable carrier, wherein said amount of the composition is effective to treat obesity in said subject. Therefore, the above-identified limitations in the claims are considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P. 608.04 to 608.04(c).

Applicants are invited to point to the descriptive support in specific pages and lines of the disclosure, as originally filed, for the limitation identified above, or alternatively, remove the new matter from the claim(s). Applicants should specifically point out the support for any amendments made to the disclosure. See MPEP 714.02 and 2163.06.

Rejection(s) under 35 U.S.C. § 112, First Paragraph (Scope of Enablement)

24) Claims 23, 24, 27, 29, 31-34, 37-39, 68, 72, 76, 80, 82, 84 and 95-97 are rejected under 35 U.S.C § 112, first paragraph, because the specification, while being enabling for a method of reducing the body weight of an insulin-requiring type II diabetic human subject having a BMI of at least or less than 27 kg/m^2 comprising subcutaneous adjunctive administration to said subject, before each meal three times a day, an amount of the amylin agonist analogue species, ^{25,28,29}Pro-h-amylin, i.e., pramlintide, for 52 weeks, and a method of reducing the body weight of an insulin-requiring human subject having type 1 diabetes mellitus having a BMI of at least 27 kg/m^2 comprising subcutaneous adjunctive administration to said subject, before each meal four times an amount of the amylin agonist analogue species, ^{25,28,29}Pro-h-amylin, i.e., pramlintide, for 20-52, wherein said pramlintide is not administered in conjunction with another obesity relief agent, wherein the body weight of said human subject is significantly reduced after 13, 26 and 52 weeks of said treatment compared to the body weight of the placebo group, does not reasonably provide enablement for a method of treating obesity in any human subject including a non-type 2 or non-type 1 diabetic human subject in need thereof, or a type 1 or type 2 diabetic human subject in need thereof who is not on insulin therapy, comprising or consisting of administering a generic amylin, a generic amylin agonist other than calcitonin or CGRP, or any 'amylin agonist analogue' or ant peptide encompassed with SEQ ID NO: 14 other than pramlintide, as claimed in a broad sense. The

specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with the claims.

Instant claims are evaluated based on *Wands* factors. Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Circ. 1988) as follows:

- The quantity of experimentation necessary (time and expense);
- The amount of direction or guidance presented;
- The presence or absence of working examples of the invention;
- The nature of the invention;
- The state of the art;
- The relative skill of those in the art;
- The predictability or unpredictability in the art; and
- The breadth of the claims.

In the instant application, the nature of the invention is pertinent to treatment of obesity in a human subject in need of such treatment comprising or consisting of administering an amylin, an amylin agonist, or an amylin agonist analogue composition, or a peptide of SEQ ID NO: 14 in an amount effective to treat obesity in said subject. As described in the instant specification, the state of the art indicates that obesity or adiposity is a chronic disease that is highly prevalent in modern society, which is strongly associated with multiple conditions including diabetes mellitus, insulin resistance, hypertension etc. The breadth of the claimed method encompasses the following. The limitation 'obesity' encompasses diabetes-associated obesity, non-diabetes-associated obesity, obesity associated with family genetics, morbid obesity, aging-associated obesity, insulin requiring obesity, obesity due to hypernutrition etc. The step recited for example in claim 33 'consists of' administering to a human subject in need of treatment of obesity an amount of a composition comprising a pharmaceutically acceptable carrier and an obesity-relief agent consisting of an amylin, an amylin agonist, or an amylin agonist analogue wherein the amount of said amylin or amylin agonist administered is about 0.01 mg to about 5 mg per day. A method of treatment 'consisting of' such an administration step *excludes* simultaneous insulin administration, or insulin administration minutes or hours before or after the administration. The method of treating obesity in a human subject in need of such treatment as claimed in the independent claim 23 'comprises' administering to said subject an amount of a composition comprising about 0.01 mg to about 5 mg per day of an amylin or an amylin agonist wherein said composition is not administered in conjunction with another obesity agent. The

method of treating obesity in a human subject in need of treatment of obesity as claimed in the independent claim 76 and the dependent claim 68 'comprises' administering to said subject an amount of a composition 'comprising' an amylin agonist analogue or a peptide having an amino acid sequence of SEQ ID NO: 14, wherein A1 is Lys, Ala, Ser, or hydrogen; B1 is Ala, Ser or Thr; C1 is Val, Leu or Ile; D1 is His or Arg; E1 is Ser or Thr; F1 is Ser, Thr, Gln, or Asn; G1 is Asn, Gln or His; H1 is Phe, Leu or Tyr; I1 is Ile, Val, Ala or Leu; J1 is Ser, Pro or Thr; K1 is Asn, Asp or Gln; X and Y are independently selected residues having side chains which are chemically bonded to each other to form an intramolecular linkage, wherein said intramolecular linkage comprises a disulfide bond, a lactam or a thioether linkage; and Z is an amino, alkylamino, dialkylamino, cycloalkylamino, arylamino, aralkylamino, alkyloxy, aryloxy or aralkyloxy; and provided that when A1 is Lys, B1 is Ala, C1 is Val, D1 is Arg, E1 is Ser, F1 is Ser, G1 is Asn, H1 is Leu, I1 is Val, J1 is Pro, and K1 is Asn; then one or more A to K1 is a D-amino acid and Z is selected from the group consisting of alkylamino, dialkylamino, cycloalkylamino, arylamino, aralkylamino, alkyloxy, aryloxy or aralkyloxy. Thus, these claims encompass the administration of a huge number of the peptide or the amylin agonist analogue variant species having the ability to treat obesity in a human in need thereof. In the method claimed in claims 68 and 76, the composition or the peptide is not administered in conjunction with another obesity relief agent. In the method claimed in claim 76, the amount of the SEQ ID NO: 14 peptide administered is generic and is effective to treat obesity, whereas in claims 68 and 72, the amount of the amylin agonist analogue administered is about 0.01 mg to about 5 mg per day. Because of the open claim language 'comprising', the composition recited in claim 76 is allowed to comprise one or more obesity relief agents or any other compounds. A composition 'comprising' a pharmaceutically acceptable carrier and about 0.01 mg to about 5 mg per day of an amylin or an amylin agonist not administered in conjunction with another obesity agent includes any element such as insulin, glucagon, an anti-diabetic agent, or a gastric emptying agent etc. The limitation 'a human subject in need of treatment of obesity' encompasses overweight, moderately obese, morbidly obese, diabetic and non-diabetic obese, insulin-requiring and insulin non-requiring obese human subject as well as a human subject with age-associated obesity. The limitations 'amylin agonist' and 'amylin agonist analogue' broadly encompass a myriad of compounds, including a peptide and a nonpeptide compound (see first full paragraph on page 13 of the original specification), non-human amylins, amylins having amino

acid modifications or substitutions, and the art-accepted amylin agonists such as calcitonin and CGRP (see lines 45-47 in column 7 of US patent 5,739,106 and claims 3 and 10 of US 5,175,145, both already of record) etc. At least a representative number of the peptide species and the amylin agonist analogue species encompassed within the scope of the instantly claimed method is *required* to be effective in treating obesity in a diabetic or non-diabetic human subject, or a morbidly or non-morbidly obese human subject when administered in conjunction with or not in conjunction with another obesity relief agent in the recited amount or dose range.

With regard to enablement, a review of the instant specification indicates that Examples 4-10 are not enabling of the claimed method of treatment. Instead, Examples 4-6 describe how to prepare selective amylin agonist analogues. Therefore, whether or not peptide variants or amylin agonist analogues encompassed within SEQ ID NO: 14 were known in the art at the time the present application was filed and that such peptide variants or analogues included those described in US patent 5,686,411 as described in the present specification at page 13, lines 23-28 and those described in US 6,114,304, is not the issue. Example 7 pertains to the evaluation of *in vitro* binding of compounds to amylin receptors whereas Example 8 pertains to the determination of amylin agonist activity of the compounds as measured by soleus muscle assay. Examples 9 and 10 describe methods of measuring gastric emptying using phenol red and tritiated glucose gastric emptying assays. However, what are claimed are not amylin agonist analogues or a method of making them, or using them in *in vitro* assays as described in Examples 4-10 of the instant specification, but a method of treating obesity in a mammal in need of treatment for obesity by administering *in vivo* an amount of an amylin, amylin agonist, amylin agonist analogue, or any peptide encompassed within SEQ ID NO: 14 effective to treat obesity as claimed. Example 3 of the instant specification is limited to a demonstration that the human subjects of the study are those with a history of type 2 diabetes mellitus, who *required* insulin treatment. Body weight-wise, i.e., obesity-wise, these patients are described as having a BMI of at least 27.0 kg/m^2 or less than 27.0 kg/m^2 before admission into the study. The only amylin agonist analogue species or the peptide species that was administered in the instant invention was ^{25,28,29}Pro-h-amylin, also known as pramlintide. Groups of type 2 diabetic 'patients' were given separate mealtime pramlintide, 30 micrograms TID; 75 micrograms TID, or 150 micrograms TID subcutaneously, before each meal three times a day.

Patients *remained on their insulin, usual diet, and exercise regimens*. The study period was 52 weeks, and the outcome was determined by comparing the mean body weight of the treated diabetic subjects with the mean body weight of the *placebo subjects*. See Tables V-VII. Thus, the originally filed specification at Example 3 and Tables V-VII describes a statistically significant reduction in the mean baseline weight seen after the subcutaneous administration of specific amounts of one specific peptide or amylin agonist analogue species, pramlintide, three times a day, to type II diabetic subjects for 52 weeks, wherein said pramlintide administration was accompanied with the continued use of insulin. Example 2 of the instant specification is limited to a demonstration that the human subjects of the study are those with a history of type 1 diabetes mellitus, who *required* insulin treatment. Body weight-wise, i.e., obesity-wise, these patients are described as having a BMI of at least 27.0 kg/m^2 before admission into the study. The only amylin agonist analogue species that was administered in the instant invention was ^{25,28,29}Pro-h-amylin, also known as pramlintide. Groups of type 1 diabetic patients were given subcutaneous adjunctive administration, before each meal four times a day, 30 micrograms of pramlintide for 20 weeks followed by either 30 or 60 micrograms of pramlintide QID up to week 52, of an amylin agonist which is ^{25,28,29}Pro-h-amylin, i.e., pramlintide. See Tables II-IV. Thus, the originally filed specification at Example 2 and Tables II-IV describes a statistically significant reduction in the mean baseline weight seen after the subcutaneous administration of specific effective amounts of one specific amylin agonist analogue species, pramlintide, four times a day, to type I diabetic subjects for 52 weeks, wherein said pramlintide administration was accompanied with the continued use of insulin. However, this single enabled embodiment is not representative of the full scope of the claims which broadly encompasses the administration of any amylin, any amylin agonist, or any of a plethora of non-pramlintide amylin agonist analogues, including the multiple variants encompassed within SEQ ID NO: 14, in the treatment of obesity in diabetic and non-diabetic patients not on insulin treatment. This is critically important, because there is no predictability at the time of the invention that if one used an amylin, amylin agonist, or a non-pramlintide amylin agonist analogue in place of Applicants' pramlintide in type 2 diabetic or non-diabetic overweight or obese subjects who are on or not on insulin treatment, or morbidly obese human subjects who are on or not on insulin therapy, the administered amylin, amylin agonist, or non-pramlintide amylin agonist analogue would bring about significant or clinically

meaningful obesity-treating effect. Neither the state of the art *at the time of the invention*, nor the instant specification as originally filed, provides specific guidance and direction with regard to the use of a generic amylin, or a non-pramlintide or non-calcitonin amylin agonist, or a non-pramlintide amylin agonist analogue including any variant of SEQ ID NO: 14 as recited, to treat obesity in any human subject in need of treatment for obesity.

Upon consideration of the evidence as a whole and analysis of all of the *Wands* factors, the instantly claimed method is viewed as being non-enabled with regard to the full scope. It should be noted that the scope of the required enablement varies inversely with the degree of predictability involved. A single embodiment may provide broad enablement in cases involving predictable factors. However, in applications directed to inventions in arts where results are unpredictable, the disclosure of a single species does not provide an adequate basis to support generic claims. MPEP § 2164.03. However, in cases involving unpredictable factors, such as most chemical reactions and physiological activity, more may be required. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity). See also *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *In re Vaeck*, 947 F.2d 488, 496, 20 USPQ2d 1438, 1445 (Fed. Cir. 1991). This is because it is not obvious from the disclosure of one species, what other species will work. In the instant case, it is not obvious from the disclosure of the administration of pramlintide species in the treatment of obesity in type 2 diabetic humans, what other non-pramlintide amylin agonist analogues or SEQ ID NO: 14 peptide variant species would work in treating obesity in diabetic or non-diabetic humans in need of treatment of obesity. It should be noted that predictability or unpredictability is one of the *Wands* factors to be considered for enablement or lack thereof under 35 U.S.C § 112, first paragraph. The instantly claimed invention is in an area of art that is unpredictable. Amylin, and a sufficient number of non-pramlintide peptide or amylin agonist analogues, are not enabled as obesity relief agents in the instantly claimed method. With regard to the therapeutic use of amylin, the state of the art indicates the difficulty, the undesirable pharmacological properties, *and* the impracticability of using amylin, including human amylin, clinically as 'a therapeutic agent'. For instance, Baron *et al.* (*Current Drug Targets – Immune, Endocrine & Metabolic Disorders* 2(1): 63-82, 2002, already of record) taught the following with regard to the clinical use of amylin as a therapeutic agent:

> Clinical use of amylin as a therapeutic agent is considered impractical because of its instability in

> solution and its propensity to aggregate and adhere to surfaces, properties that hamper the manufacturing, formulation, and storage of this peptide as a drug. Pramlintide is a synthetic, equipotent analogue of human amylin in which the undesirable pharmacological properties of human amylin (insolubility, tendency to self-aggregate) have been overcome by replacement of the three amino acid residues .... with prolines ....

Ratner *et al.* (*Diabetes Technol. Ther.* 4: 51-61, 2002, already of record) provide a similar teaching (see paragraph bridging the two columns on page 52):

> Native human amylin is not ideal for clinical use because of the peptide's poor solubility and propensity to aggregate.

Applicants state that Baron *et al.* and Ratner *et al.* support enablement of the claimed invention (see page 28 of Applicants' amendment filed 10/23/07), but fail to explain how these references enable a method of administering amylin or any non-pramlintide amylin agonist analogue to a human for treating obesity.

A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, *unless* there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. Assuming that sufficient reason for such doubt exists, a rejection for failure to teach how to make and/or use will be proper on that basis. *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971).
In the instant case, one of the reasons for doubting the objective truth of the statements comes from Applicants' own statement. For example, with regard to the state of the art at the time of the invention, Applicants have previously gone on the record with the following (see pages 9, 13 and 14 of Applicants' Appeal Brief filed July 2000 in the prior application 08/870,762) [Emphasis in original]:

> .... THE RINK PATENT PROVIDES THAT AMYLIN AND AMYLIN AGONISTS ADMINISTERED AS DESCRIBED AND CLAIMED IN THE PRESENT APPLICATION HAVE "NO MEASURABLE EFFECT" ON FOOD INTAKE.
>
> .... the Rink patent reports that a 1.0 μg/kg dose (equivalent to about 70μg/dose in an adult human) had no effect on food intake.

The Rink patent that is being referred to by Applicants in the Appeal Brief is US 5,739,106 (already of record). Note that the above-mentioned about 70 μg/dose in an adult human is encompassed

within the therapeutic amount range of about 0.01 to about 5 mg, as recited in instant claims 23 and 33. Applicants have not advanced any arguments with regard to this issue raised in the previous Office Action. Thus, in view of the above-cited acknowledgment of the failure of amylin to have any effect on food intake, one of skill in the art would look into Applicants' specification for guidance and direction. However, the instant specification fails to show that human or non-human amylin, or a composition comprising or consisting of the same, was in fact stable, soluble and/or non-aggregating enough to be 'therapeutic' in a method of treating obesity upon administration in any amount and by any route, with or without concurrent insulin therapy, to a diabetic or non-diabetic human subject in need of treatment for obesity. Applicants have previously acknowledged that obesity is a complex, chronic, multifactorial disease that has been the subject of decades of research. Applicants have acknowledged that there are contradictions and confusion in the relevant art. See pages 22 and 23 of Applicants' response filed 09/02/04. Although Example 9 of the instant specification describes the gastric emptying assay and the effect of specific amounts of 'amylin' (as opposed to the amylin agonist analogue SEQ ID NO: 14) on gastric emptying in diabetic rats, and Examples 7 and 8 describe the receptor binding and soleus assays of some amylin variants, of the various biologic activities or functions attributed to amylin or pramlintide, which precise activity or activities provide for, or are associated with obesity relief in the 'human subject' genus has not been precisely identified. Of the various screenable activities, whether one activity, all the activities, or a specific combination of activities, are responsible for the obesity-relief function(s) is neither known in the art nor established within the instant specification, absent which one of skill in the art cannot practice the claimed invention without engaging in a considerable amount of undue experimentation. A mere screening of art-known amylin agonist analogue species falling within the genus of SEQ ID NO: 14 using the conventional screening assays does not enable one to reproducibly practice the claimed method of treatment. Whether or not the various amylin agonist analogue species or peptide variant species encompassed within the scope of the SEQ ID NO: 14 genus have the *required* obesity relief function(s) is neither known nor can it be predicted. While there is no requirement for Applicants to enable all of the peptide variant species or amylin agonist analogue species encompassed within the claimed invention, enablement of a reasonable number such species in the claimed method is required particularly in view of the unpredictability. Applicants have previously stated that neither the amylin

art nor the obesity art suggested or indicated an approach to trying an amylin or an amylin agonist (let alone an amylin agonist analogue or the peptide variant) for weight reduction or treatment of obesity. See bottom of page 57 of Applicants' response filed 09/02/04. With regard to what was known in the art at the time of the invention or thereafter, Applicants stated that Frishman *et al.* ((*In*: *Cardiovascular Pharmacotherapeutics*. (Eds) Frishman WH *et al.* McGraw-Hill Health Professions Division, New York, Chapter 48, pages 1093-1114, February 1997, of record) 'only' concluded that 'the potential role of amylin in weight reduction "awaits clinical investigation"'. See the full paragraph on page 85 of Applicants' response filed 09/02/04. Applicants have recognized the importance of the unpredictability previously. For example, with regard to the gastric emptying function/activity and obesity, Applicants have previously taken the position that there is no agreement on the effect of gastric emptying in obesity. Applicants pointed to various reports and stated that the role of gastric emptying in obesity was uncertain and controversial at the time of filing of the instant application, as well as before and after. See page 37 of Applicants' response filed 09/02/04. Applicants mentioned of the Minnesota Medical Association's recent reporting that gastric emptying is useful in treating diabetics, but researchers are 'uncertain' whether it will produce weight loss. See page 37 of Applicants' response filed 09/02/04. Applicants have gone on the record previously stating that any and all compounds having any gastric emptying activity are *not* necessarily useful for treating obesity, let alone one that is being evaluated for use in the treatment of diabetes. See lines 4-6 on page 85 of Applicants' response filed 09/02/04. With the art-known fact that obesity is a complex, chronic and multifactorial disease and with the precise amylin or pramlintide activity contributing to obesity relief being unknown at the time of the invention, there is no predictability that the recited peptide variants or amylin agonist analogues having the recited amino acid substitutions or chemical modifications encompassed within the genus of SEQ ID NO: 14 would be therapeutically functional as effective obesity-relief agents in a human subject. Furthermore, the effects these various amino acid substitutions and/or chemical modifications would have on the activity of amylin agonist analogues or peptides which contribute to the reported undesired side effects, including recurrent nausea and vomiting and excessive anorexia, and the undesired properties such as insolubility and tendency toward aggregation, are also unpredictable. The various amino acid substitutions and/or chemical modifications encompassed within SEQ ID NO: 14 can potentially render the amylin agonist

analogue species or peptide variant species more insoluble and aggregating than amylin and unacceptably nausea- or vomiting-inducing with no effect on food intake or obesity. In sum, the instant specification simply lacks a concrete *in vivo* showing that a representative number of amylin agonist analogue species or peptide species encompassed within the SEQ ID NO: 14 genus has obesity-relieving function in any human subject in need of the claimed method of treatment.

With regard to the quantity of experimentation needed, the standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: 'is the experimentation needed to practice the invention undue or unreasonable'. That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). In the instant case, no guidance or direction has been provided in the instant specification so that one could predict which of the amylin agonist analogue species other than pramlintide or which of the peptide variant species of claim 76 other than pramlintide would have the requisite therapeutic effect against obesity. Because there is no way to predict *a priori* which amylin agonist analogues or peptides from the specification or the chemical structures alone would be therapeutically active against obesity in diabetic or non-diabetic humans subjects, including morbidly obese human subjects, an extraordinary amount of trial and error experimentation is required to identify the obesity-treating amylin agonist analogues or the peptides. Assuming *arguendo* that the experimentation required is routine, and if one of skill in the art screens innumerable non-pramlintide amylin agonist analogue species or the peptide variant species currently encompassed within the recited genus, including those disclosed in Examples 4-6 of the instant invention, using receptor binding assays and assays for amylin activity, there is absolutely no predictability that a non-pramlintide amylin agonist analogue or peptide variant mimicking an effect of amylin would have obesity-treating effect, or food intake-reducing effect, given the Applicants' admission that amylin itself has no effect on food intake. Given this and the lack of showing within the instant specification, the obesity-treating effect of any amylin or any non-pramlintide amylin agonist analogue or peptide variant having amylin activity, administered alone or as an adjunct to insulin therapy, to an obese diabetic or obese non-diabetic human subject, is simply not predictable. Applicants have provided no guidance with regard to the use of extraordinarily large genus of amylins, amylin agonists, amylin agonist analogues, and peptides

in the treatment of obesity in humans. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) states: 'The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art'. The amount of guidance or direction refers to that information in the application, as originally filed, that teaches exactly how to make or *use* the invention. The more is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling' (MPEP 2164.03). MPEP also states that physiological activity can be considered inherently unpredictable. Whether the specification would have been enabling *as of the filing date* involves consideration of the nature of the invention, the state of the prior art, and the level of skill in the art. The initial inquiry is into the nature of the invention, i.e., the subject matter to which the claimed invention pertains. The nature of the invention becomes the backdrop to determine the state of the art and the level of skill possessed by one skilled in the art. The state of the prior art is what one skilled in the art would have known, *at the time the application was filed*, about the subject matter to which the claimed invention pertains. The relative skill of those in the art refers to the skill of those in the art in relation to the subject matter to which the claimed invention pertains *at the time the application was filed*. See MPEP § 2164.05(b). The post-filing abstracts of Aronne *et al.* (*Obesity* 14: A17, 2006 – Applicants' IDS) and Smith *et al.* (*Diabetes* 56: A88, 2007 – Applicants' IDS) submitted by Applicants are silent about the diabetic or non-diabetic status of the subjects included in the study. Both are limited to the use of the single amylin agonist analogue species, pramlintide in the method described therein. The post-filing teachings of Aronne *et al.* (*J. Endocrinol. Metabol.* 92: 2977-2983, 2007 – Applicants' IDS) and Smith *et al.* (*J. Am. J. Physiol. Endocrinol. Metabol.* 293: 620-627, 2007 – Applicants' IDS) submitted by Applicants are also limited to the use of one amylin agonist analogue species, pramlintide, for reducing caloric intake and meal size, or for reducing body weight. These two post-filing publications support the Office's position on lack of enablement of the full scope of the instant claims by confirming that even about a decade after the effective filing date of the instant application, the only amylin agonist analogue species within the recited broad genus

that is being used for inducing weight loss in humans is pramlintide. None of these post-filing references and abstracts represents the state of the art *at the time of filing*. Contrary to Applicants' allegation, a *prima facie* case of lack of scope of enablement has been established by providing sufficient references and specific technical reasons along with the documentation of Applicants' own previous statement indicating that an amylin, amylin agonist, or amylin agonist analogue having an amylin activity does not necessarily have an effect on food or caloric intake, and therefore does not necessarily have an anti-obesity effect. Thus, in view of level of skill, the state of the art at the time of the invention, and the information in the specification, one of skill would *not* expect that the recited genus could be used in that manner without undue experimentation. For the reasons delineated above and due to the lack of specific direction or guidance within the instant specification, the breadth of the claims, the absence of working examples enabling the full scope, the art-recognized unpredictability factor, and the quantity of the experimentation necessary, a considerable amount of non-routine undue experimentation would have been required to reproducibly practice the full scope of the invention, as claimed. Instant claims do not meet the scope of enablement provisions of 35 U.S.C. § 112, first paragraph. The scope of enablement provided to one skilled in the art is not commensurate with the scope of protection sought by the instant claims.

Rejection(s) under 35 U.S.C. § 102

25) The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> **(b)** the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> **(e)** the invention was described in-
> **(2)** a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

26) Claims 23, 24, 27, 29, 31, 33, 34, 37-39, 80 and 82 are rejected under 35 U.S.C § 102(b) as being anticipated by Kolterman *et al.* (WO 96/40220, already of record) ('220) as evidenced by Tsanev (*Vutr. Boles* 23: 12-17, 1984, abstract, already of record).

Instant claims are granted the effective filing date of the instant application due to the new matter identified above.

It is noted that the inventorship of the Kolterman ('220) publication (Kolterman, Thompson, and Mullane) is non-identical with the inventorship of the instant application (Duft and Kolterman). Therefore, the publication of Kolterman *et al.* ('220) is proper prior art under 35 U.S.C. § 102(a). See MPEP 2132 III.

It is further noted that the limitation 'treating obesity' is defined in the instant specification as including 'controlling weight for cosmetic purposes in humans, that is to control body weight to improve bodily appearance', or preventing 'the onset of symptoms or complications, alleviating the symptoms or complications'. See second paragraph on page 9 of the substitute specification. It is noted that the patient population used in the instant invention to treat obesity by the administration of the recited amount of pramlintide is insulin-requiring Type 2 diabetics. See Example 1 of the instant specification.

Kolterman *et al.* ('220) taught a method of administering to an insulin-taking type II diabetic human subject a dose of 10, 30, 50, 60 or 150 micrograms per day (i.e., the amount falling in the range recited in the instant claims) of the amylin agonist composition, pramlintide or $^{25, 28, 29}$pro-h-amylin, also known as AC137. The composition consists of pramlintide and a pharmaceutically acceptable carrier, and is administered in single or multiple doses, for example, of about 30 micrograms QID or about 60 micrograms TID or QID. See pages 9-11; paragraph bridging pages 20 and 21; page 21; first paragraph in page 19; lines 8-10 on page 19; and first row reciting 'Insulin-Treated Patients' in each Table. Pramlintide is administered subcutaneously 1-4 times a day before meals (see pages 9 and 22). Kolterman *et al.* ('220) additionally taught that the presence of obesity is a characteristic of 'most patients with Type II diabetes mellitus' (see page 10). Kolterman *et al.* ('220) taught the benefit of obtaining weight loss in Type II diabetic patients by teaching that hyperglycemia associated with Type II diabetes can be reversed or ameliorated by weight loss sufficient to restore the sensitivity of the peripheral tissues to insulin (see pages 7, first paragraph), thus teaching that Type II diabetic patients are in need of weight loss or treatment of obesity. Thus, the very active step of the instantly claimed method was disclosed and practiced by Kolterman *et al.* ('220) in 1996 in the very same patient population used by Applicants in Example 1 of the instant application. The prior art method is the *same* as the instantly claimed method in terms of the amylin agonist or the amylin agonist analogue, the amylin agonist composition or the

amylin agonist analogue composition (pramlintide) administered, and the insulin-taking Type II diabetic patient population used (80-90% of whom are known in the art to be intrinsically obese as taught by Tsanev - see Tsanev's abstract), the subcutaneous route of administration used, the dose and the daily frequency of the amylin agonist pramlintide administered, and the administration step prior to meals. Given Tsanev's express disclosure that 80 to 90% of type II diabetic patients are intrinsically obese, and given Kolterman's ('220) express recognition that obesity is a characteristic of 'most patients with Type II diabetes mellitus' and the indication that these patients are in need of weight loss, Kolterman's ('220) method of subcutaneous administration of pramlintide to at least one Type II diabetic patient in an amount that falls within the range recited in the instant claims, necessarily serves as the claimed method of treating obesity and therefore anticipates the instantly claimed method. Since 80-90% of Type II diabetic patients are known in the art to be obese, at least one of Kolterman's ('220) type II diabetic patients to whom pramlintide composition is administered, necessarily qualifies as a human subject in need of treatment of obesity as recited in the instant claims. Since the structural limitations of the instantly claimed method and all of the criteria required by the instant claims are clearly met by the teachings of Kolterman *et al.* ('220), Kolterman's ('220) method is expected to serve necessarily as the instantly claimed method and is expected to bring about the obesity-treating effect. The Office's position that Kolterman's ('220) method is the same as the Applicants' claimed method is based upon the fact that the method step, the pramlintide compound administered, the amount of the compound administered, the route by which the compound is administered, and the at least one intrinsically obese diabetic human patient to which the pramlintide compound is administered, are the *same* in the two methods. The art-recognized intrinsic obesity being prevalent in 80 to 90% of diabetic patients as disclosed by Tsanev (see abstract), Kolterman's ('220) method of administration of the above-identified therapeutically effective amount (i.e., about 30 micrograms QID, or about 60 micrograms TID or QID, or a dose of 10, 30, 50, 60 or 150 micrograms per day) of the amylin agonist ^{25,28,29}Pro-human amylin to at least one intrinsically obese type 2 diabetic human subject anticipates the instant claims. Given that the method step of the Kolterman's ('220) method and the instant claims are the same, Kolterman's ('220) method is expected to bring about an obesity-treating effect in the intrinsically obese pramlintide-treated type II diabetic patient. Since the Office does not have the facilities for

examining and comparing Applicants' claimed method with that of the prior art, the burden is on Applicants to show a novel difference between the claimed product and the product of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald et al.*, 205 USPQ 594. MPEP 2112 refers to *In re Best* to explain that something which is old does not become patentable upon the discovery of a new property; 'the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977)'. Since the prior art clearly teaches the instantly claimed method, any assertions of specific functional properties attributed to the amylin agonist pramlintide in the claimed method are merely inherent and do not necessarily make the claimed method patentable.

Claims 23, 24, 27, 29, 31, 33, 34, 37-39, 80 and 82 are anticipated by Kolterman *et al.* ('220). The publication of Tsanev is **not** used as a secondary reference in combination with the reference of Kolterman *et al.* ('220), but rather is used to show that every element of the claimed subject matter is disclosed by Kolterman *et al.* ('220), with the unrecited limitation(s) being inherent as evidenced by the state of the art. See *In re Samour* 197 USPQ 1 (CCPA 1978). 'To serve as an anticipation when the reference is silent about the asserted inherent characteristic, such gap in the reference may be filled with recourse to extrinsic evidence. Such evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill.' *Continental Can Co. USA v. Monsanto Co.*, 948 F.2d 1264, 1268, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991). Note that as long as there is evidence of record establishing inherency, failure of those skilled in the art to contemporaneously recognize an inherent property, function or ingredient of a prior art reference does not preclude a finding of anticipation. *Atlas Powder Co. v. IRECO Inc.*, 190 F.3d 1342, 1349, 51 USPQ2d 1943, 1948 (Fed. Cir. 1999). See MPEP 2124. Tsanev's extrinsic evidence makes clear that the missing descriptive matter, i.e., prevalence of obesity in at least one of Kolterman's ('220) diabetic subjects administered with pramlintide, is necessarily present in the thing described by Kolterman *et al.* ('220). The method of Kolterman *et al.* ('220) clearly anticipates the claimed method of the instant invention, because Kolterman *et al.* ('220) taught the very step of the instantly claimed method in the very same human patient population. The alleged failure of Kolterman ('220) to expressly mention

treatment of obesity as a goal is irrelevant. To the extent the method embodiment in the claimed invention achieves treatment of obesity, so does the method of Kolterman's ('220). Where the result is a necessary consequence of what was deliberately intended, it is of no import that the article's authors did not appreciate the results. See *Mehl/Biophile International Corp. v. Milgraum*, U.S. Court of Appeals Federal Court, 52 USPQ2d 1303 and 1306, 192 F3d 1362, 1999 citing *W.L. Gore & Assocs. v. Garlack, Inc.*, 721 F.2d 1540, 1548, 220 USPQ 303, 309 (Fed. Cir. 1983).

27) Claims 23, 24, 29, 33, 34 and 38 are rejected under 35 U.S.C § 102(e)(2) as being anticipated by Gaeta *et al.* (US 5,686,411, already of record) ('411) as evidenced by Tsanev (*Vutr. Boles* 23: 12-17, 1984, abstract, already of record).

The limitation 'method ... comprising ..... wherein said compound is not administered in conjunction with another obesity relief agent' in claim 23, and the limitation 'composition comprising an obesity relief agent .... carrier' in claim 33 do not exclude the presence of an anti-diabetic agent, insulin, glucagon, a gastric emptying-inhibiting agent, etc. in the recited composition.

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 C.F.R 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention 'by another', or by an appropriate showing under 37 C.F.R 1.131.

Gaeta *et al.* ('411) taught a method of treatment of diabetes mellitus in a mammal, including a patient seen by a medical practitioner, i.e., a human, comprising the administration to said mammal of a therapeutically effective amount of the amylin agonist of claim 19, ^{25,28,29}Pro-human amylin (SEQ ID NO: 1 or pramlintide). See claims 34, 35 and 19; and lines 45-53 in column 7 of the '411. Gaeta *et al.* ('411) taught the 'therapeutically effective amount' of the amylin agonist to include the dosage units of 0.1 to 5 mg or 0.5 to 1.0 mg of the amylin agonist. See lines 53-59 in column 8. The amount effective to treat obesity encompassed in the instant claims as described in the instant application, for example, about 0.01 milligrams to about 5 milligrams per day, about 0.05 milligrams to about 2 milligrams per day, or 300 micrograms per dose, falls in the range of therapeutically effective amount of the amylin agonist disclosed in the '411 patent. Lines 9-14 of

column 3 of the U.S. patent '411 describe that the limitation 'diabetes mellitus' includes insulin-requiring diabetes mellitus and that the administration is of amylin agonist analogue *alone*. The amylin agonist composition comprises a pharmaceutical carrier and the amylin agonist without insulin or glucagon. See lines 9-11 in column 7 and lines 37-39 in column 8. Given the art-known prevalence of intrinsic obesity in 80% to 90% of diabetic patients as disclosed by Tsanev (see abstract), at least one of the diabetic patients administered with the amylin agonist ^{25,28,29}Pro-human amylin in the method disclosed by the '411 patent qualifies a man patient in need of treatment for obesity. Given that the method step of the '411 patent and the instant claims are the same, the amylin agonist, ^{25,28,29}Pro-human amylin, administered and the amount administered are the same, the method of the '411 patent is expected to bring about a therapeutic effect, weight gain-inhibiting effect, and weight loss-inducing effect in the intrinsically obese ^{25,28,29}Pro-human amylin-treated insulin-requiring diabetic patient of Gaeta ('411) as defined in the instant invention. Since the structural limitations of the instantly claimed method and all of the criteria required by the instant claims are met by the teachings of the '411 patent, Gaeta's ('411) method is expected to serve necessarily as the instantly claimed method and is expected to bring about the obesity-treating effect, weight gain-inhibiting effect, or weight loss-inducing effect. The Office's position that Gaeta's ('411) method is the same as the Applicants' claimed method is based upon the fact that the method step, the amylin agonist, ^{25,28,29}Pro-human amylin administered, the amount of the ^{25,28,29}Pro-human amylin administered, and the at least one intrinsically obese diabetic human patient to whom the ^{25,28,29}Pro-human amylin is administered, are the *same* in the two methods. The art-recognized intrinsic obesity being prevalent in 80 to 90% of diabetic patients as disclosed by Tsanev (see abstract), Gaeta's ('411) method of administration of the above-identified therapeutically effective amount (i.e., 0.1 to 5 mg, or 0.5 to 1.0 mg) of the amylin agonist ^{25,28,29}Pro-human amylin to at least one intrinsically obese type 2 diabetic human subject anticipates the instant claims. Given that the method step of the Gaeta's ('411) method and the instant claims are the same, Gaeta's ('411) method is expected to bring about the weight gain-inhibiting, weight loss-causing, or obesity-treating effect against the intrinsic obesity in the ^{25,28,29}Pro-human amylin-treated, insulin-requiring human diabetic patient. Since the Office does not have the facilities for examining and comparing Applicants' claimed method with that of the prior art, the burden is on Applicants to show a novel

difference between the claimed method and the method of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald et al.*, 205 USPQ 594. MPEP 2112 refers to *In re Best* to explain that something which is old does not become patentable upon the discovery of a new property; 'the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977)'. Since the prior art clearly teaches the instantly claimed method, any assertions of specific functional properties attributed to the amylin agonist ^{25,28,29}Pro-human amylin in the claimed method are merely inherent and do not necessarily make the claimed method patentable.

Claims 23, 24, 29, 33, 34 and 38 are anticipated by Gaeta *et al.* ('411). The publication of Tsanev is **not** used as a secondary reference in combination with the reference of Gaeta *et al.* ('411), but rather is used to show that every element of the claimed subject matter is disclosed by Gaeta *et al.* ('411) with the unrecited limitation(s) being inherent as evidenced by the state of the art. See *In re Samour* 197 USPQ 1 (CCPA 1978). 'To serve as an anticipation when the reference is silent about the asserted inherent characteristic, such gap in the reference may be filled with recourse to extrinsic evidence. Such evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill.' *Continental Can Co. USA v. Monsanto Co.*, 948 F.2d 1264, 1268, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991). Note that as long as there is evidence of record establishing inherency, failure of those skilled in the art to contemporaneously recognize an inherent property, function or ingredient of a prior art reference does not preclude a finding of anticipation. *Atlas Powder Co. v. IRECO Inc.*, 190 F.3d 1342, 1349, 51 USPQ2d 1943, 1948 (Fed. Cir. 1999). See MPEP 2124. Tsanev's extrinsic evidence makes clear that the missing descriptive matter, i.e., prevalence of obesity in at least one of Gaeta's ('411) insulin-requiring diabetic subjects administered with ^{25,28,29}Pro-human amylin, is necessarily present in the thing described by Gaeta *et al.* ('411). The method of Gaeta *et al.* ('411) clearly anticipates the claimed method of the instant invention, because Gaeta *et al.* ('411) taught the very step of the instantly claimed method in the very same diabetic human patient. The alleged failure of Gaeta *et al.* ('411) to expressly mention treatment of obesity as a goal is irrelevant. To the extent the method embodiment in the claimed invention achieves treatment of obesity, so does the method of

Gaeta *et al.* ('411). Where the result is a necessary consequence of what was deliberately intended, it is of no import that the article's authors did not appreciate the results. See *Mehl/Biophile International Corp. v. Milgraum*, U.S. Court of Appeals Federal Court, 52 USPQ2d 1303 and 1306, 192 F3d 1362, 1999 citing *W.L. Gore & Assocs. v. Garlack, Inc.*, 721 F.2d 1540, 1548, 220 USPQ 303, 309 (Fed. Cir. 1983).

28) Claims 23, 24, 27, 29, 31, 33, 34, 37-39, 80 and 82 are rejected under 35 U.S.C § 102(b) as being anticipated by Kolterman *et al.* (*Diabetologia* 39: 492-499, April, 1996, already of record) (Kolterman *et al.*, 1996) as evidenced by Itasaka *et al.* (*Psychiatr. Clin. Neurosci.* 54: 340-341, June 2000, already of record).

It is noted that the human patient in need of the recited treatment according to the instant invention is expressly identified in the instant specification as one having a body weight of 79 kg. A 70 kg patient is not excluded from the scope of the instant invention 'as a human subject in need thereof', but is expressly included. The recited therapeutic amount range of 'about 0.1 milligrams per day to about 1 milligram per day', or 'about 0.01 to about 5 mg/day', or 0.03 to about 5 mg/day of the amylin agonist or amylin agonist analogue, pramlintide, administered is specifically "for a 70 kg patient". See lines 4-8 of page 23 of the substitute specification; and paragraph bridging pages 23 and 24 and lines 3-7 on page 24 of Applicants' response filed December 2002. A diabetic human patient having a baseline BMI of up to 27.0 kg/m^2 is not excluded from the scope of the instant invention 'as a human subject in need thereof', but is expressly included. See lines 26 and 27 of page 35 of the instant specification.

It is further noted that the claimed method of treating obesity in a human subject in need thereof encompasses alleviating the 'symptoms' of the disorder, i.e., obesity. See the last paragraph on page 9 of the substitute specification. The substitute specification at paragraph bridging pages 7 and 8 characterizes 'increased appetite' as a sign strongly associated with obesity (see second paragraph). Thus, increased appetite and therefore, increased food intake is viewed as a 'symptom' of obesity. It is further noted that the limitation 'treating obesity' is defined in the instant specification as including 'controlling weight for cosmetic purposes in humans, that is to control body weight to improve bodily appearance', or preventing 'the onset of symptoms or complications, alleviating the symptoms or complications'. See second paragraph on page 9 of the substitute

specification.

Kolterman *et al.* (1996) taught a method of subcutaneous administration of 30, 100, or 300 μg of pramlintide composition or AC137 (i.e., $^{25, 28, 29}$pro-h-amylin or SEQ ID NO: 1), a human amylin analogue, to human patients with insulin-dependent diabetes mellitus or IDDM who are on insulin. Pramlintide is administered three times daily for a period of 14 days. See abstract; and page 493. The mean body weight ± SEM of diabetic patients included in Kolterman's (1996) method who were administered subcutaneously with 30 micrograms, 100 micrograms, and 300 micrograms of pramlintide, three times a day for 14 days, was 70.6 ± 2.7, 74.4 ± 2.5, and 75.7 ± 2.6 respectively. Therefore, the 70.6 to 75.7 kg insulin-taking diabetic patients from Kolterman's (1996) study qualify as human subjects in need of treatment for obesity as recited in the instant claims. Additionally, even BMI-wise, Kolterman's (1996) diabetic subjects meet the limitation 'a human subject .... in need of treatment for obesity' as recited in the instant claims, because the diabetic subjects included in Kolterman's method (1996) had a BMI of up to 27. See second full paragraph under 'Subjects, materials and methods. Therefore, Kolterman's (1996) diabetic subjects having a BMI at least in the range of 24 up to 27 do qualify as diabetic subjects in need of treatment for obesity in light of what is known in the art. For example, Itasaka *et al.* teach that a BMI of 24.0 to 26.4 represents mild obesity and 26.4 and heavier (i.e., including a BMI of 26.4 to 27) represents obesity in humans (see abstract of Itasaka *et al.*). Kolterman's (1996) pramlintide composition did not comprise another obesity relief agent, but consisted of or consisted essentially of pramlintide. The pramlintide composition was injected subcutaneously to the human patients (see 'Study design') and therefore is expected to inherently contain a pharmaceutically acceptable carrier therein. The amount administered was 30 micrograms three times a day to 'about 0.1 milligrams' or 300 micrograms per day. See 'Study design'; Table 1; and paragraph there below. Kolterman's (1996) subcutaneous administration of a therapeutically effective amount of the amylin agonist ^{25,28,29}Pro-human amylin to diabetic human subjects on insulin weighing 70 kg or more, or having a BMI falling in the BMI range of 24 up to 27, anticipates the instant claims. Thus, the very active step recited in the instantly claimed method was disclosed and practiced by Kolterman *et al.* in April, 1996. Given that the method step in Kolterman's (1996) method and the instant claims are the *same*, and the amylin agonist analogue pramlintide administered and its amount administered are the *same*,

Kolterman's (1996) method is expected to necessarily bring about the same weight gain-inhibiting (i.e., maintaining of existing body weight) or weight loss-inducing therapeutic effect in Kolterman's (1996) pramlintide-treated diabetic patients who are on insulin. Since the Office does not have the facilities for examining and comparing Applicants' claimed method with that of the prior art, the burden is on Applicants to show a novel difference between the claimed product and the product of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald et al.*, 205 USPQ 594. MPEP 2112 refers to *In re Best* to explain that something which is old does not become patentable upon the discovery of a new property; 'the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977)'. Since the prior art clearly teaches the claimed method, any assertions of specific functional properties attributed to the amylin agonist pramlintide in the claimed method are merely inherent and do not necessarily make the claimed method patentable. The prior art method of administering the above-explained amount of the amylin agonist ^{25,28,29}Pro-human amylin (pramlintide or SEQ ID NO: 1) to insulin-taking diabetic human subjects weighing 70 kg or more, and/or having a BMI falling in the range of 24 up to 27 necessarily serves as the Applicants' method of treating obesity by inhibiting weight gain or inducing weight loss, as claimed currently.

Claims 23, 24, 27, 29, 31, 33, 34, 37-39, 80 and 82 are anticipated by Kolterman *et al.* (1996). The publication of Itasaka *et al.* is **not** used as a secondary reference in combination with the reference of Kolterman *et al.* (1996), but rather is used to show that every element of the claimed subject matter is disclosed by Kolterman *et al.* (1996) with the unrecited limitation(s) being inherent as evidenced by the state of the art. See *In re Samour* 197 USPQ 1 (CCPA 1978). 'To serve as an anticipation when the reference is silent about the asserted inherent characteristic, such gap in the reference may be filled with recourse to extrinsic evidence. Such evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill.' *Continental Can Co. USA v. Monsanto Co.*, 948 F.2d 1264, 1268, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991). Note that as long as there is evidence of record establishing inherency, failure of those skilled in the art to contemporaneously recognize an inherent property, function or ingredient of a prior art reference does not preclude a

finding of anticipation. *Atlas Powder Co. v. IRECO Inc.*, 190 F.3d 1342, 1349, 51 USPQ2d 1943, 1948 (Fed. Cir. 1999). See MPEP 2124. Itasaka's extrinsic evidence makes clear that the missing descriptive matter, i.e., prevalence of obesity in at least one of Kolterman *et al.* (1996) insulin-taking diabetic subjects administered with ^{25,28,29}Pro-human amylin, is necessarily present in the thing described by Kolterman *et al.* (1996). The method of Kolterman *et al.* (1996) clearly anticipates the claimed method of the instant invention, because Kolterman *et al.* (1996) taught the very step of the instantly claimed method in the diabetic human patient. The alleged failure of Kolterman *et al.* (1996) to expressly mention treatment of obesity as a goal is irrelevant. To the extent the method embodiment in the claimed invention achieves treatment of obesity, so does the method of Kolterman *et al.* (1996). Where the result is a necessary consequence of what was deliberately intended, it is of no import that the article's authors did not appreciate the results. See *Mehl/Biophile International Corp. v. Milgraum*, U.S. Court of Appeals Federal Court, 52 USPQ2d 1303 and 1306, 192 F3d 1362, 1999 citing *W.L. Gore & Assocs. v. Garlack, Inc.*, 721 F.2d 1540, 1548, 220 USPQ 303, 309 (Fed. Cir. 1983).

29) Claims 23, 24, 27, 29, 33, 34, 37 and 38 are rejected under 35 U.S.C § 102(e)(2) as being anticipated by Beumont *et al.* (US 5,321,008, already of record) ('008) as evidenced by Tsanev (*Vutr. Boles* 23: 12-17, 1984, abstract, already of record).

It is noted that the limitation 'method ... comprising ..... wherein said compound is not administered in conjunction with another obesity relief agent' in claim 23, and the limitation 'composition comprising an obesity relief agent .... carrier' in claim 33 do not exclude the presence of an anti-diabetic agent, insulin, glucagon, a gastric emptying-inhibiting agent, etc. in the recited composition. It is further noted that 'amylin agonist' is defined in the instant specification as a peptide or non-peptide compound that mimics the effect of amylin. See third paragraph of the specification under 'Summary of the Invention'. Calcitonin and CGRP are described in the instant specification as sharing the food intake-suppressing action or effect of peripherally or centrally administered amylin. See first full paragraph on page 9 of the originally filed specification.

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This

rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 C.F.R 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention 'by another', or by an appropriate showing under 37 C.F.R 1.131.

Beumont *et al.* ('008) taught a method of subcutaneous administration to an insulin-requiring human who suffers from Type 1 or Type 2 diabetes mellitus a therapeutically effective amount of an amylin agonist *alone* such as calcitonin, or calcitonin and insulin, contained in a pharmaceutically acceptable carrier. See claims 11, 7, 13 and 4; lines 14-17 in column 5; lines 8-11 and 49-54 in column 12; and lines 34 and 35 in column 2. Claim 11 of the '008 patent is directed to the method of administering a therapeutically effective amount of the amylin agonist calcitonin to an insulin-requiring human with diabetes mellitus. The 'therapeutically effective amount' taught by Beumont *et al.* ('008) includes the typical dosage units of about 0.1 to 1 mg of calcitonin. See first full paragraph in column 13. The amount effective to treat obesity, the amount effective to inhibit weight gain, or the amount effective to induce weight loss encompassed in the instant claims as described in the instant application of about 0.01 milligrams to about 5 milligrams per day, about 0.05 milligrams to about 2 milligrams per day, or 300 micrograms per dose, falls within the range of the therapeutically effective amount disclosed in the '008 patent. Given the art-known prevalence of intrinsic obesity in 80% to 90% of diabetic patients as disclosed by Tsanev (see abstract), at least one diabetic patient used in the method disclosed in the '008 patent qualifies as a human patient in need of treatment for obesity. Therefore, the method of the '008 patent comprising the administration of about 0.1 to 1 mg of calcitonin to a diabetic human anticipates the instant claims. Given that the method step of the '008 patent and the instant claims is the same, and the amylin agonist administered and the amount administered are the same as the ones described in the instant specification, the method of the '008 patent is expected to bring about a obesity-treating effect, weight gain-inhibiting effect, or weight loss-inducing effect in Beumont's intrinsically obese calcitonin-treated diabetic patient as defined in the instant invention. Since the structural limitations of the instantly claimed method and all of the criteria required by the instant claims are met by the teachings of the '008 patent, Beumont's ('008) method is expected to serve necessarily as the instantly claimed method and is

expected to bring about the obesity-treating effect, weight gain inhibiting effect, or weight loss-inducing effect. The Office's position that Beumont's ('008) method is the same as the Applicants' claimed method is based upon the fact that the method step, the amylin agonist calcitonin administered and its amount administered, the subcutaneous route by which the amylin agonist is administered, and the at least one intrinsically obese diabetic human patient to which the amylin agonist is administered, are the *same* in the two methods. The art-recognized intrinsic obesity being prevalent in 80 to 90% of diabetic patients as disclosed by Tsanev (see abstract), Beumont's ('008) method of administration of the above-identified therapeutically effective amount (i.e., dosage units of about 0.1 to 1 mg) of the amylin agonist calcitonin to at least one intrinsically obese type 2 diabetic human subject anticipates the instant claims. Given that the method step of the Beumont's ('008) method and the instant claims are the same, Beumont's ('008) method is expected to bring about the weight gain-inhibiting, weight loss-causing or obesity-treating effect in the intrinsically obese calcitonin-treated insulin-requiring human diabetic patient of Beumont's ('008) patent. Since the Office does not have the facilities for examining and comparing Applicants' claimed method with that of the prior art, the burden is on Applicants to show a novel difference between the claimed method and the method of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald et al.*, 205 USPQ 594. MPEP 2112 refers to *In re Best* to explain that something which is old does not become patentable upon the discovery of a new property; 'the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977)'. Since the prior art clearly teaches the instantly claimed method, any assertions of specific functional properties attributed to the amylin agonist calcitonin in the claimed method are merely inherent and do not necessarily make the claimed method patentable.

Claims 23, 24, 27, 29, 33, 34, 37 and 38 are anticipated by Beumont *et al.* ('008). The publication of Tsanev is **not** used as a secondary reference in combination with the reference of Beumont *et al.* ('008), but rather is used to show that every element of the claimed subject matter is disclosed by Beumont *et al.* ('008) with the unrecited limitation(s) being inherent as evidenced by the state of the art. See *In re Samour* 197 USPQ 1 (CCPA 1978). 'To serve as an anticipation when

the reference is silent about the asserted inherent characteristic, such gap in the reference may be filled with recourse to extrinsic evidence. Such evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill.' *Continental Can Co. USA v. Monsanto Co.*, 948 F.2d 1264, 1268, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991). Note that as long as there is evidence of record establishing inherency, failure of those skilled in the art to contemporaneously recognize an inherent property, function or ingredient of a prior art reference does not preclude a finding of anticipation. *Atlas Powder Co. v. IRECO Inc.*, 190 F.3d 1342, 1349, 51 USPQ2d 1943, 1948 (Fed. Cir. 1999). See MPEP 2124. Tsanev's extrinsic evidence makes clear that the missing descriptive matter, i.e., prevalence of obesity in at least one of Beumont's insulin-requiring diabetic subjects administered with calcitonin, is necessarily present in the thing described by Beumont *et al.* ('008). The method of Beumont *et al.* ('008) clearly anticipates the claimed method of the instant invention, because Beumont *et al.* ('008) taught the very step of the instantly claimed method in the very same diabetic human patient. The alleged failure of Beumont *et al.* ('008) to expressly mention treatment of obesity as a goal is irrelevant. To the extent the method embodiment in the claimed invention achieves treatment of obesity, so does the method of Beumont *et al.* ('008). Where the result is a necessary consequence of what was deliberately intended, it is of no import that the article's authors did not appreciate the results. See *Mehl/Biophile International Corp. v. Milgraum*, U.S. Court of Appeals Federal Court, 52 USPQ2d 1303 and 1306, 192 F3d 1362, 1999 citing *W.L. Gore & Assocs. v. Garlack, Inc.*, 721 F.2d 1540, 1548, 220 USPQ 303, 309 (Fed. Cir. 1983).

Remarks

30) Claims 23, 24, 27, 29, 31-34, 37-39, 68, 72, 76, 80, 84 and 95-97 stand rejected.

31) Applicants' amendments necessitated the new ground(s) of rejection presented in this Office action. **THIS ACTION IS MADE FINAL.** Applicants are reminded of the extension of time policy as set forth in 37 C.F.R 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

32) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. The Fax number for submission of amendments, responses and/or papers is (571) 273-8300, which receives transmissions 24 hours a day and 7 days a week.

33) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (in USA or CANADA) or 571-272-1000.

34) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, Shanon Foley, can be reached on (571) 272-0898.

S. DEVI, PH.D.
PRIMARY EXAMINER

January, 2008